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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/732,782	12/10/2003	Stephen Hsu	275.0007 0101	6883

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EXAMINER	
PHAM, AUDREY S	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/732,782	HSU ET AL.	
	Examiner	Art Unit	
	Audrey S. Pham	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *November 15, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 12-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Re: Hsu *et al.*

Claims 1-35 are pending

Claims 1-9, 12-35 have been withdrawn from further consideration by the examiner under 37 CFR 1. 142(b) as being drawn to non-elected inventions.

Claims 10-11 are under consideration.

Examiner's Response to Applicant's Election/Restriction

The Election filed on November 15, 2005, in response to the Office Action Requirement for Restriction dated October 19, 2005 is acknowledged and has been entered. Applicant elected, with traverse, Group V, Claims 10-11, drawn to a method of determining the therapeutic effectiveness of an agent comprising contacting cells with an agent determining the p57/KIP2 levels and comparing the normal cells with the cancer cells.

The traversal is on the ground that it would not be unduly burdensome to search groups I-IV, XIII and XIV with group V because a search and examination for the methods of Groups I-IV and the methods of Groups XIII and XIV would be co-extensive with the search for Group V. Therefore, Groups I-IV, XIII, XIV should be rejoined with Group V.

These arguments have been carefully considered but are not deemed persuasive for the following reasons:

The criteria for establishing a serious burden are set forth in MPEP §808.02. To establish a serious burden, one of the following can be shown: (1) a separate classification, (2) a separate status in the art when the inventions are classified together, or (3) a different field of search. For the reasons of record (Office Action dated October 19, 2005), the requirement for serious burden is met with regard the restriction requirement between Groups I-IV, V, XIII and XIV.

The restriction requirement is deemed proper and, is therefore, made FINAL.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ito *et al.* (*Oncology*, Oct. 2001, Vol. 61, pages 221-225, IDS) in view of Massague *et al.* (International Publication Number WO 96/31534, October 1996) and in further view of Allen-Hoffmann *et al.* (US Patent No 6,214,567, April 2001).

Claim 10 is drawn to a method of determining the therapeutic effectiveness of an agent, comprising contacting normal cells with the agent; determining the p57/KIP2 level in the normal cells after contacting with the agent; contacting cancer cells with the agent; determining the p57/KIP2 level in the cancer cells after contacting with the agent; and comparing the p57/KIP2 level in the normal cells after contacting with the agent to the p57/KIP2 level in the cancer cells after contacting with the agent; wherein a higher p57/KIP2 level in the normal cells compared to the p57/KIP2 level in the cancer cells indicates the agent is effective for the treatment of cancer. Claim 11 further limits claim 10 wherein the normal cells and cancer cells are cultured together.

Ito *et al.* establish that p57/KIP2 is a tumor marker in hepatocellular carcinoma (abstract) and that the p57/KIP2 expression level is associated with tumor progression (page 223, col 1, starting last line). Ito *et al.* do not teach screening agents using p57/KIP2.

Massague *et al.* teach (page 6, lines 16-20) the treatment of cancer by administering agents that target the activity of p57/KIP2. Massague *et al.* further teach (page 29, lines 10-24) screening for therapeutic agents that are capable of increasing or decreasing the level of expression of p57/KIP2 comprising preparing cell extracts from control and agent-treated cell populations, isolating p57/KIP2 from the cell extracts and quantifying the amount of p57/KIP2 inhibitor activity in the control and agent-treated cell extracts.

Neither Ito *et al.* nor Massague *et al.* teach co-culturing normal cells and cancer cells together.

Allen-Hoffmann *et al.* teach (col 4, lines 46+) co-culturing of human keratinocytes with human squamous cell carcinoma (SCC) cells to identify potential cytostatic and chemopreventive agents with specific tumor selectivity.

It would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to combine the teachings of Ito *et al.* and Massague *et al.* to screen for diagnostic agents that target p57/KIP2 because Ito *et al.* established that p57 contributes to the progression of HCC. One would have been motivated to combine the teachings because it was well known in the art, at the time the invention was made, to determine the therapeutic effectiveness of an agent by comparing the levels of p57/KIP2 in normal and cancer cells because Massague *et al.* teach (page 6, lines 27-31) that a lesser amount of active cyclin-CDK complex formed in the presence of an agent than in the absence of the agent indicate that the agent is capable of specifically enhancing the ability of p57/KIP2 to inhibit the activation of cyclin-CDK complex. Further, it can be advantageous to screen agents by using p57/KIP2 in co-cultures because Allen-Hoffmann *et al.* teach (Col 5, line 54+) that such co-cultures are useful for: (1) screening for novel cytostatic inhibitors of tumor repopulation, (2) determining patient-specific responses to chemotherapy or radiotherapy prior to treatment, and (3) developing novel, biologic therapeutic agents. One of ordinary skill in the art would have reasonably expected to obtain a benefit upon combining Ito's with Massague's and Allen-

and Allen-Hoffmann's teachings because the combined teachings had been demonstrated in the prior art to be reasonably predictive of screening for therapeutic agents.

Conclusion

No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Audrey S. Pham whose telephone number is (571) 272-3323. The examiner can normally be reached during the hours of 8:30 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached during business hours at the telephone number: (571) 272-0787. The fax number for the organization, where this application or proceeding is assigned, is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Audrey S. Pham
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Art Unit 1642

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER